

### Remarks

Claims 29, 30, 33-42, 45, 48-56, 122-175, 177-186, 188-197, 199-208 and 210-219 are pending in the instant application upon entry of the present amendment. Claims 122-129, 131-138, 140-147, 149-156, 158-165 and 167-175 are allowed. Claims 35-42, 45, 49-56, 130, 139, 148, 157, 166, 175, 179-186, 190-197, 201-208 and 212-219 are rejected. Claims 29, 30, 33, 34, 48, 177, 178, 188, 189, 199, 200, 210 and 211 are objected to.

Previously presented claims 27, 28, 31, 32, 43, 44, 46, 47, 102-121, 176, 187, 198 and 209 have been cancelled without prejudice or disclaimer, and Applicants reserve the right to pursue such cancelled subject matter in one or more subsequent applications. Previously presented claims 29, 45, 177, 188, 199 and 210 have been rewritten in independent form. Previously presented claims 33, 35, 37, 38, 40, 48, 49, 51, 52, 54, 179, 181, 182, 184, 190, 192, 193, 195, 201, 203, 204, 206, 212, 214, 215 and 217 have been rewritten so as to no longer depend from claims cancelled herein. Previously presented claims 130, 139, 148, 157, 166, 175, 186, 197, 208 and 219 have been currently amended to recite "under conditions such that the polypeptide encoded by said nucleic acid molecule is expressed." Support for these amendments are found throughout the specification and claims as originally filed and previously presented. Accordingly, no new matter has been entered by amendment.

In summarizing the Office Action the Examiner indicates that claim 175 is both allowed and rejected. In order to minimize confusion, Applicants shall treat claim 175 as if it is rejected.

35 U.S.C. § 101

The Examiner states that “[a]ny objection or rejection of record that is not expressly repeated in this action has been overcome by Applicant’s response and withdrawn.” See, Paper No. 34, page 1. As no rejection of claims for lack of utility is expressly repeated in the instant Office Action, Applicants understand that the Examiner has withdrawn the rejections previously of record under 35 U.S.C. § 101. However, in presenting an analysis of the presently claimed invention under 35 U.S.C. § 101 the Examiner alleges:

the utility of a protein encoded by a nucleic acid of the instant invention in the identification of agonists and antagonists thereto is limited to a protein that provides an authentic response, which is predictive of an *in vivo* physiological response.

See, Paper No. 34, page 1. Applicants respectfully traverse.

Preliminarily, Applicants agree with the Examiner in the analysis of the assertion on page 46 of the specification, “that the protein of the instant invention can be employed to identify antagonists thereto, which would be expected to be anti-inflammatory, constitutes a credible, specific and substantial utility.” See, Paper No. 34, page 1.

However, Applicants respectfully point out that the specification discloses other credible, specific and substantial utilities for molecules as presently claimed. These utilities include, among other things, diagnostic applications for detecting disease. More specifically, the specification discloses that:

The present invention also provides diagnostic assays such as quantitative and diagnostic assays for detecting levels of DR3 or DR3-V1 protein. Thus, for instance, a diagnostic assay in accordance with the invention for detecting overexpression of DR3 or DR3-V1, or soluble form thereof, compared to normal control tissue samples may be used to detect the presence of tumors.

*See*, specification, page 5, lines 10-14. Furthermore, the present application discloses that molecules of the present invention are involved in "[d]iseases associated with increased cell survival, or the inhibition of apoptosis," including cancers (such as follicular lymphomas), autoimmune disorders (such as rheumatoid arthritis) and graft versus host disease (GVHD). *See*, specification at page 149, lines 12-20.

Based on the complete disclosure that Applicants have provided, one of ordinary skill in the art would understand that the claimed polynucleotides have many uses, including use in the diagnosis of diseases and/or disorders associated with aberrant cell survival, *e.g.*, cancers, and use in the diagnosis of diseases and/or disorders of the cells in which they are expressed, *e.g.*, lymphocytes. Accordingly, one of ordinary skill in the art would appreciate that the claimed polypeptides are useful in the diagnosis of diseases associated with aberrant survival of lymphocytes including cancers such as follicular lymphomas, autoimmune disorders such as rheumatoid arthritis, and inflammatory disorders such as GVHD.

As acknowledged by the Examiner, a Declaration Under 37 C.F.R. § 1.132 executed by Dr. Thi-Sau Migone was filed by Applicants on November 21, 2002 in the instant application. The Examiner alleges that the declaration of Dr. Thi-Sau Migone

does not support a specific and substantial utility for an isolated nucleic acid encoding all or a portion of a protein that does not provide an authentic response because the information derived therefrom would have no immediate practical utility."

*See*, Paper No. 34, pages 1-2. Applicants respectfully disagree.

In the declaration, Dr. Migone states that DR3 is expressed at very low levels in normal resting T cells and at very low levels in normal B cells. *See*, Declaration, ¶ 21. Furthermore, Dr. Migone states that data reported by an independent third party shows that

DR3 is "abundantly expressed" in each of eleven distinct clinical isolates of follicular lymphoma. *See*, Declaration, ¶ 22. Dr. Migone concludes that the evidence of record, "confirms that DR3 overexpression is useful as a diagnostic marker for certain lymphoid cancers such as acute lymphoblastic leukemia and follicular lymphoma," and that "one of ordinary skill in the art would find it credible that DR3 is useful as a diagnostic marker for certain cancers, as disclosed in the Application." *See*, Declaration, ¶¶ 21 and 24.

Applicants respectfully point out that the use of the claimed polynucleotides in the diagnosis of certain cancers such as follicular lymphoma, does not require that the claimed polynucleotides encode a full-length or functional molecule, let alone one that produces "an authentic response." Indeed, all that is required of the claimed polynucleotides is that they may be used by one of skill in the art in determining and/or comparing the level of expression of DR3 in healthy and diseased tissues. In this context, useful polynucleotides include those which may function as PCR primers or hybridization probes. Neither of these functions require that the polynucleotide be either full-length or capable of encoding a receptor which produces "an authentic response." Accordingly, Applicants respectfully contend that, in direct contradiction to the assertions of the Examiner, the declaration of Dr. Thi-Sau Migone does "support a specific and substantial utility for an isolated nucleic acid encoding all or a portion of a protein that does not provide an authentic response." *See*, Paper No. 34, pages 1-2.

In light of the above comments and explanations it is clear that the instant application provides an appropriate example of a situation "where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition" and therefore provides a specific utility. (M.P.E.P. § 2107.01(I)[2100-32].) Additionally, this utility is substantial, since "[a]n assay that measures the presence of a material which

has a stated correlation to a predisposition to the onset of a particular disease condition ... defines a 'real world' context of use." *See*, MPEP § 2107.01(I) [2100-32].

Based on the above, it is clear that each of the claimed polynucleotides satisfy the requirements of 35 U.S.C. § 101. The assertion that DR3 can be used in diagnostic applications to detect disclosed cancers is specific and substantial, and as stated by Dr. Migone, one of ordinary skill in the art would find such an assertion credible. Accordingly, Applicants respectfully contend that the Examiner's analysis of the instant invention under 35 U.S.C. § 101, in light of the declaration of Dr. Migone, is fundamentally flawed.

**Claim Rejections Under 35 U.S.C. § 112, first paragraph**

The Examiner has rejected claims 27, 28, 31, 32, 35 to 47, 49 to 56, 102 to 121, 176, 179 to 187, 190 to 198, 201 to 209 and 212 to 219 under 35 U.S.C. § 112, first paragraph, as the specification allegedly "does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims." *See*, Paper No. 34, page 2. The rejection is respectfully traversed.

Preliminarily, Applicants respectfully point out that rejected claims 27, 28, 31, 32, 43, 44, 46, 47, 102-121, 176, 187, 198 and 209 have been cancelled without prejudice or disclaimer, thereby obviating their rejection. Rejected dependent claims 29, 45, 177, 188, 199 and 210 have been rewritten in independent form including the relevant limitations of their original base claims and any intervening claims, and are therefore allowable as indicated by the Examiner. *See*, Paper No. 34, page 2. Furthermore, rejected dependent claims 35-42, 49-56, 179-186, 190-197, 201-208 and 212-219 have been rewritten so as to

depend from allowable rewritten independent claims 29, 45, 177, 188, 199 and 210 as currently amended herein. The listed amendments have obviated the present rejection of claims 27, 28, 31, 32, 35 to 47, 49 to 56, 102 to 121, 176, 179 to 187, 190 to 198, 201 to 209 and 212 to 219 under 35 U.S.C. § 112, first paragraph.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 27, 28, 31, 32, 35 to 47, 49 to 56, 102 to 121, 176, 179 to 187, 190 to 198, 201 to 209 and 212 to 219, under 35 U.S.C. § 112, first paragraph, for lack of enablement.

**Claim Rejections Under 35 U.S.C. § 112, second paragraph**

The Examiner has rejected claims 130, 139, 148, 157, 166, 175, 186, 197, 208 and 219 under 35 U.S.C. § 112, second paragraph as allegedly “being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.” More specifically, the Examiner alleges that “the identity of the polypeptide being produced by the claimed method is unclear. The act of culturing a host cell inherently results in the production of thousands of different polypeptides.” *See*, Paper No. 34 at page 4. The rejection is respectfully traversed.

Preliminarily, Applicants respectfully point out that the presently rejected claims 130, 139, 148, 157, 166, 175, 186, 197, 208 and 219 have been currently amended to recite “under conditions such that the polypeptide encoded by said nucleic acid molecule is expressed.” Support for these amendments is found throughout the specification and claims as originally filed and previously presented.

Applicants respectfully contend that the present amendment obviated the Examiner’s rejection of these claims as being indefinite as it is clear what protein is being

produced by the claimed method. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 130, 139, 148, 157, 166, 175, 186, 197, 208 and 219, under 35 U.S.C. § 112, second paragraph, as being indefinite.

### **Claim Objections**

The Examiner has objected to claims 29, 30, 33, 34, 48, 177, 178, 188, 189, 199, 200, 210 and 211 as allegedly “being dependent on a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.” *See*, Paper No. 34 at page 4. The Examiner’s objection is respectfully traversed.

Applicants respectfully point out that as described above, claims 29, 30, 33, 34, 48, 177, 178, 188, 189, 199, 200, 210 and 211 have been rewritten as independent claims, or so as to depend from rewritten independent claims, incorporating all of the limitations of their original base claims and any intervening claims.

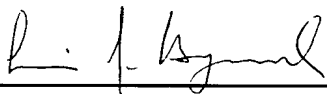
In light of the above amendments Applicants respectfully request reconsideration and withdrawal of the instant objection to claims 29, 30, 33, 34, 48, 177, 178, 188, 189, 199, 200, 210 and 211.

### ***Conclusion***

Applicants respectfully request that the amendments and remarks of the present response be entered and made of record in the present application. The present application is believed to be in condition for allowance. Early notice to that effect is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below. If a fee is required in connection with this paper, please charge Deposit Account No. 08-3425 for the appropriate amount.

Respectfully submitted,

Dated: November 3, 2003

  
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Enclosures  
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